IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (JLH) **DEMAND FOR JURY TRIAL**
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA, Defendant/Counter-Plaintiffs, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC., Plaintiff/Counter Defendants.	[redacted] [redacted]

NS'S RESPONSES TO SAREPTA THERAPEUTICS, INC. AND THE UNIVERSITY OF WESTERN AUSTRALIA'S RESPONSIVE CONCISE STATEMENT OF FACTS

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TABLE OF ABBREVIATIONS

Abbreviation	Description
'851 Patent	U.S. Patent No. 9,994,851
'590 Patent	U.S. Patent No. 10,227,590
'827 Patent	U.S. Patent No. 10,266,827
'361 Patent	U.S. Patent No. 9,708,361
'092 Patent	U.S. Patent No. 10,385,092
'461 Patent	U.S. Patent No. 10,407,461
'106 Patent	U.S. Patent No. 10,487,106
'741 Patent	U.S. Patent No. 10,647,741
'217 Patent	U.S. Patent No. 10,662,217
'322 Patent	U.S. Patent No. 10,683,322
ASO	Antisense oligonucleotide
Bold and Italic	Emphasis added unless indicated otherwise
Br-1	NS's Memorandum of Law in Support of Its Motion for Partial Summary Judgment No. 1 Regarding Invalidity of the UWA Patents (D.I. 400)
Br-2	NS's Memorandum of Law in Support of Its Motion for Partial Summary Judgment No. 2 Regarding Infringement of Certain NS Patents (D.I. 403)
Br-3	NS's Memorandum of Law in Support of Its Motion for Partial Summary Judgment No. 3 Regarding Its Breach of Contract Claim (D.I. 406)
Br-4	NS's Memorandum of Law in Support of Its Motion for Partial Summary Judgment No. 4 Regarding No Anticipation (D.I. 410)
Br-5	NS's Memorandum of Law in Support of Its Motion for Partial Summary Judgment No. 5 Regarding No Inequitable Conduct (D.I. 415)
DMD	Duchenne muscular dystrophy
Ex. ____	Exhibit ____[1]
MCA	Mutual Confidentiality Agreement (D.I. 2-1)
NS	Plaintiff/Counter-Defendants Nippon Shinyaku Co., Ltd. and NS Pharma, Inc.
NS Patents	U.S. Patent Nos. 9,708,361; 10,385,092; 10,407,461; 10,487,106; 10,647,741; 10,662,217; 10,683,322

[1] Refers to Exhibits to the accompanying Declaration of Megan E. Dellinger in Support of Sarepta Therapeutics, Inc. and The University of Western Australia's Oppositions to Plaintiff/Counter-Defendants' Motions for Summary Judgment and Motions to Exclude Certain Opinions and Testimony of Steven F. Dowdy, Ph.D. and Andrew Hirshfeld.

Abbreviation	Description
PMO	Phosphorodiamidate morpholino oligomer
Popplewell 2010	Popplewell, et al., Comparative analysis of antisense oligonucleotide sequences targeting exon 53 of the human DMD gene: Implications for future clinical trials, 20 NEUROMUSCULAR DISORDERS 102–110 (2010)
Popplewell ’212	U.S. Patent Publication No. 2010/0168212
POSA	Person of ordinary skill in the art
Sarepta	Defendant/Counter-Plaintiff Sarepta Therapeutics, Inc.
Sazani 2010	Sazani, P., et al., Safety Pharmacology and Genotoxicity Evaluation of AVI-4658, *Int’l J. of Toxicology*, 29(2):143-156 (2010)
Sazani ’586	International Patent Publication No. WO 2010/048586
Sazani ’591	U.S. Patent Application Publication No. US2010/0130591
RSOF	Responsive Concise Statement of Facts in Support of Sarepta Therapeutics, Inc. and the University of Western Australia’s Opposition to NS’s Summary Judgment Motions
UWA	Counter-Plaintiff The University of Western Australia
Wilton Patents	U.S. Patent Nos. 9,994,851; 10,227,590; and 10,266,827

OUTSIDE COUNSEL EYES ONLY – SUBJECT TO PROTECTIVE ORDER

Plaintiff Nippon Shinyaku Co. Ltd. And NS Pharma (together "NS") respectfully submits the following response to the Responsive Concise Statement of Facts submitted by Sarepta Therapeutics, Inc. in opposing NS's Motions for Summary Judgment Nos. 1-5 (D.I. 470). NS includes Sarepta's headings solely for clarity, and does not concede their characterizations.

I. *NS'S MOTION #1:* INVALIDITY OF THE UWA PATENTS

A. NS's Response to Sarepta's Concise Counterstatement of Facts

1. The Shared Specification of the Wilton Patents

RESPONSE TO 1.1. Admitted.

RESPONSE TO 1.2. Denied. Dr. Hastings disputes that the UWA Patents disclose a "hot spot" region amenable for exon skipping, and details various evidence belying Sarepta's contention, including [redacted] D.I. 427-5 (Hastings Rpt.), ¶¶ 66-87; D.I. 427-7 (Hastings Reply), ¶¶ 22-26. Dr. Hastings also disputes whether a POSA would interpret the activity reported in Table 39 for SEQ ID NO: 195 as disclosing the activity of SEQ ID NO: 195 individually, rather than in a "cocktail" with other AOs. D.I. 427-5 (Hastings Rpt.), ¶¶ 94-95, 98-99.

RESPONSE TO 1.3. Denied. Dr. Hastings disputes that the UWA Patents disclose a "hot spot," as noted in NS's Response to 1.2 above. D.I. 427-5 (Hastings Rpt.), ¶¶ 50, 57-59, 66-87; D.I. 427-7 (Hastings Reply), ¶¶ 22-26. NS admits that the graphic shown is from Dr. Dowdy's report.

RESPONSE TO 1.4. Admitted that Sarepta's Vyondys 53® (golodirsen) and NS's Viltepso® (viltolarsen) are the only AOs approved by FDA for treating DMD in patients with mutations amenable to exon 53 skipping and are complementary to positions 36 to 60 and 36 to 56, respectively. Denied that the work described in the UWA Patents defined an amenable region for golodirsen and viltolarsen. Dr. Hastings disputes that the UWA Patents disclose a "hot spot," as noted in NS's Response to 1.2 above. D.I. 427-5 (Hastings Rpt.), ¶¶ 50, 57-59, 66-87; D.I. 427-7 (Hastings Reply), ¶¶ 22-26. No one in the UWA laboratory [redacted] D.I. 471-2 (Ex. 7, Wilton Dep.) at 28:9-18, 31:2-6, 31:18-25.

RESPONSE TO 1.5. The first sentence is denied. Dr. Hastings disputes whether the UWA Patents provide meaningful "guidance." D.I. 427-5 (Hastings Rpt.), ¶¶ 50, 57-59, 66-87; D.I. 427-

7 (Hastings Reply), ¶¶ 57-58 (specification has limited disclosures and teaches that "the named inventors did not consider the rational design methodologies used for the specification's Examples to be 'reliable'"), ¶ 73 (noting additional work necessary), ¶ 96 (the specification "does not describe any of the experimental procedures or techniques employed"). Admitted that the prior art discloses certain methods of synthesizing and screening individual AOs and otherwise denied.

2. The Wilton Patents Read by a POSA

RESPONSE TO 1.6. Denied. While certain claim limitations impose structural requirements (*e.g.*, those specifying the "base sequence," "thymine bases," and "morpholino" chemistry), these requirements do **not** implement any particular structure commonly shared by all claimed AOs. D.I. 427-5 (Hastings Rpt.), ¶¶ 61-66; D.I. 427-7 (Hastings Reply), ¶¶ 28 (n. 14), 38-40; *see also* D.I. 400 at 11-15 and supporting evidence. Consistent with the Court's construction, NS also disputes that "antisense oligonucleotide" imposes a complementarity requirement not otherwise recited in the claims. D.I. 427-7 (Hastings Reply), ¶¶ 10-14, 21, n. 2; D.I. 421 at 1-3; D.I. 248 at 7-12.

RESPONSE TO 1.7. Denied. The claimed genus is vast, (D.I. 401, SOF ¶¶ 5-9), and highly unpredictable, (*id.* ¶¶ 10-15). Dr. Hastings also disputes these purported facts. D.I. 427-5 (Hastings Rpt.), ¶¶ 45-65; D.I. 427-7 (Hastings Reply), ¶¶ 18-20, 22-40.

RESPONSE TO 1.8. Admitted that the quoted statements are from Dr. Dowdy's reports and the UWA Patents and otherwise denied. Denied that Dr. Dowdy's opinions regarding claim scope would not change. His footnote is conclusory, (D.I. 427-2, ¶ 37 n.4), and squarely at-odds with [redacted] (D.I. 401, SOF ¶¶ 5-9, 14).

RESPONSE TO 1.9. Admitted that the quoted statements are from Dr. Hastings's report and deposition, and that Dr. Dowdy provided the graphic shown. Otherwise denied because Sarepta mischaracterizes Dr. Hastings's opinions. Dr. Hastings's calculations [redacted]

[redacted] D.I. 427-5 (Hastings Rpt.), ¶¶ 45-48. They do not [redacted] disclosed by the specification "[redacted] D.I. 427-7 (Hastings Reply), ¶¶ 10-14, 21, n. 2. Also, the '851 Patent's additional "target region is within" requirement modifies the region to which the "base sequence"—not the entire "antisense oligonucleotide" is complementary. '851 Patent, cl. 1; D.I. 427-7 (Hastings Reply), ¶ 18, n. 6.

3. Predictability of Exon 53 Skipping ASOs in View of the Wilton Patents

RESPONSE TO 1.10. Admitted that the quoted language is in the document cited, but otherwise denied. Dr. Hastings disputes that the UWA Patents disclose a "hot spot," and details post-priority date evidence showing lack of recognition of any +23+69 "hot spot." D.I. 427-5 (Hastings Rpt.), ¶¶ 50, 57-59, 66-87; D.I. 427-7 (Hastings Reply), ¶¶ 22-26.

RESPONSE TO 1.11. Admitted that Dr. Hastings [redacted] and that Dr. Dowdy offers the quoted opinion, otherwise denied. Dr. Hastings testified that she "[redacted]" (D.I. 471-1 (Ex. 4, Hastings Dep.) at 107:22-108:3), and explained [redacted]" (D.I. 427-5 (Hastings Rpt.), ¶ 101).

RESPONSE TO 1.12. Admitted that Dr. Dowdy analyzed post-priority date AOs and stated as quoted, otherwise denied. Dr. Dowdy's purported examples are each 100% complementary, and do not reflect the breadth of the claims, which undisputedly encompass candidate AOs having at least four mismatches. D.I. 427-2 (Dowdy Rebuttal), ¶¶ 75-94; D.I. 401 (SOF ¶ 8). Dr. Hastings disputes the conclusions Dr. Dowdy draws from this data, and opines that it demonstrates a lack of recognition of the claimed genus. D.I. 427-7 (Hastings Reply), ¶¶ 53-65).

II. *NS'S MOTION #2:* INFRINGEMENT OF NS PATENTS

Sarepta did not provide any counter statements of fact to which NS needs to respond.

III. *NS'S MOTION #3:* BREACH OF CONTRACT

A. NS's Responses to Sarepta's Concise Counterstatement of Facts

1. Mr. Jarosz's Damages Range

RESPONSE TO 3.1. Admitted. NS denies that Sarepta is allowed to claim a different measure of damages than that Mr. Jarosz claimed in his expert report.

2. NS Materially Breached the MCA

RESPONSE TO 3.2 Admitted.

RESPONSE TO 3.3 Denied. Sarepta makes legal assertions regarding what amounts to at most a technical breach of the MCA. NS disputes that the original Complaint in this action contained confidential information in violation of the MCA. *See* D.I. 44 at 4-6. Section 2.2 of the MCA expressly permits NS to use confidential information "in an action to enforce the terms of" the MCA—precisely what NS contends the instant action is.

RESPONSE TO 3.4. Admitted. NS included the confidential information based on its good faith belief that it was permitted to do so pursuant to the MCA.

RESPONSE TO 3.5 Admitted.

RESPONSE TO 3.6 Admitted. NS respectfully disagrees with Judge Stark's ruling.

RESPONSE TO 3.7 Denied. Judge Stark's ruling speaks for itself and made no mention or holding that there was any "material breach" as Sarepta asserts. *See* Sarepta Ex. 2. NS continued to include information Judge Stark ultimately struck from the then-operative pleading in an amended pleading based on its good faith belief that it was entitled to include such information pursuant to Section 2.2 of the MCA. *See* D.I. 44 at 4-6.

IV. *NS'S MOTION #4:* NO ANTICIPATION OF CERTAIN NS PATENT CLAIMS

A. NS's Responses to Sarepta's Concise Counterstatement of Facts

RESPONSE TO 4.1: Denied. '212 Popplewell discloses 24 PMOs that target different positions in exon 53 of the human dystrophin pre-mRNA. These 24 PMOs are listed in '212 Popplewell's Table 4. D.I. 471-7 (Ex. 18, '212 Popplewell) at Table 4. None of the PMOs in Table 4 is 100% complementary to the (+36+60) region of exon 53 in human dystrophin. *Id.*

RESPONSE TO 4.2: Admitted.

RESPONSE TO 4.3: Admitted that as of August 2011, a POSA would have known that 5'-TEG could be used as a 5'-end group for PMOs. Otherwise denied.

RESPONSE TO 4.4: Admitted that of August 2011, certain publications stated that the 5'-TEG modification may confer improved solubility and stability to PMOs. Otherwise denied.

V. *NS'S MOTION #5:* NO INEQUITABLE CONDUCT

A. NS's Responses to Sarepta's Concise Counterstatement of Facts

RESPONSE TO 5.1: NS admits that paragraph 219-226 of Sarepta's Counterclaims are not tested in its SOF ¶ 1. Paragraph 219-226 of Sarepta's Counterclaims (D.I. 328) are under the header "Specific Intent to Deceive the USPTO" and speak for themselves. Mr. Naoki Watanabe is a named inventor on the NS Patents and testified [redacted]. D.I. 471 Ex. 9, 40:3-5, 40:17-19, 41:8-15, 213:3-6. Mr. Watanabe was not asked to describe his understanding of what that duty entails or requires. D.I. 471 Ex. 9, 213:3-6. Mr. Watanabe testified that [redacted] (*id.*, 42:3-11), [redacted] (*id.*, 44:4-13), [redacted] (*id.*, 43:15-23), wrote i[redacted]" (*id.*, 181:1-24) and has [redacted]. *Id.*, 214:20-215:4. Sarepta did not seek a deposition of Ms. Hino to determine what role, if any, she had in prosecuting the NS Patents. And Mr. Watanabe testified that he [redacted] D.I. 471 Ex. 9, 213:15-18, 213:19–25, 214:10–19. Otherwise denied.

RESPONSE TO 5.2: NS admits that it made the argument quoted in the parenthetical during prosecution of the '361 patent, and otherwise denied. The examiner found the unexpected superiority argument "not persuasive" and disagreed with the claim of unexpected superior results. *See* D.I. 416, ¶ 6.

RESPONSE TO 5.3: NS admits that Mr. Watanabe testified [redacted]

[redacted] D.I. 471 Ex. 9, 124:6-22. Otherwise denied. Figure 16 of the NS Patents reflects that the oligonucleotide targeting positions 35 to 59 achieved higher skipping efficiency than the oligonucleotide targeting positions 36 to 60. [cite one of the NS Patents], Fig. 16.

RESPONSE TO 5.4: Denied. Mr. Watanabe testified at deposition that he [redacted]," D.I. 471 Ex. 9 at 125:22-126:4 (discussing Watanabe Ex. 22). Mr. Watanabe was not testifying generally or categorically that [redacted].

RESPONSE TO 5.5: NS admits that [redacted] D.I. 427-28, NS00000792-93. Otherwise denied. Data disclosed in Figures 16 and 17 of the NS Patents reflected that SEQ ID NO: 57 did not exhibit superior skipping to the oligonucleotide corresponding to positions 35-59. Ex. 60, (Dowdy Dep.) at 141:18-142:17, 143:1-17, 148:13-18; *see also* D.I. 427-6 (Hastings Rebuttal) ¶ 234.

RESPONSE TO 5.6: Denied. Sazani '586 discloses conjugating a PMO with a 5'-TEG moiety. Ex. 60, (Dowdy Dep.) at 170:10-22, 171:2-172:8, 173:10-16; D.I. 427-6 (Hastings Rebuttal) ¶¶ 249-250. Sazani '586 appears on face of the NS Patents as a "Reference Cited." '217 Patent at cover. The additional disclosures of Sazani 2010, such as those concerning genotoxicity and pharmacology safety studies, and the full chemical composition of AVI-4658, are not relevant to

the claims because they are outside the scope of the claims. The claims of the NS Patents do not include any limitations regarding genotoxicity or pharmacological safety. Ex. 60, (Dowdy Dep.) at 173:17-23; *see also* D.I. 427-6 (Hastings Rebuttal) ¶ 255. The PMO that is disclosed in Sazani 2010 is AVI-4658, which targets exon 51 of human dystrophin pre-mRNA. Ex. 60, (Dowdy Dep.) at 166:19-167:7, 170:23-25; *see also* D.I. 427-6 (Hastings Rebuttal) ¶ 250, n.24. Moreover, '212 Popplewell, which is listed on the face of the NS Patents as a "Reference Cited" ('217 Patent at cover) states "the advantages of a PMO is that it has excellent safety profiles." Ex. 60, (Dowdy Dep.) at 174:5-11. In 2010, a POSA would have considered PMOs to be generally safe. *Id.* at 175:3-6.

RESPONSE TO 5.7: Denied. The documents and testimony cited reflect that NS [redacted]. Mr. Watanabe testified [redacted] Ex. 62, (Watanabe Dep.) at 181:25-182:8. Mr. Watanabe testified that [redacted]" Ex. 62, (Watanabe Dep.) at 183:1-5.

RESPONSE TO 5.8: Denied. The disclosures of Sazani 2010 that were relevant to the claims of the NS Patent were cumulative of information disclosed to the PTO. D.I. 427-6 (Hastings Rebuttal) ¶¶ 248-254.

CERTIFICATE OF SERVICE

The undersigned certifies that on January 26, 2024, a copy of the foregoing, which was filed under seal, was served via electronic mail on the following counsel of record:

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